Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 1-49 and 53 have been cancelled without prejudice. Claims 50 and 55-58 have been amended. New claims 59-67 have been added. Claims 50-52 and 54-67 are pending. No new matter has been added by the way of the above amendments. Support for the amendments to claims 50 and 67 is found in paragraphs [0042] and [0061]. The limitation of at least 95% (and the requirement that the polypeptide have the amino acid sequence of SEQ ID NO: 2) falls within the scope of the disclosure of at least 85% similar to a non-mutant translation initiation factor eIF4E of SEQ ID NO: 2. Paragraph [0035] supports new claims 59. Claims 60-66 are supported by paragraph [0042].

Plant virus diseases can damage leaves, stems, roots, fruits, seed, or flowers, and are responsible for a considerable percentage of economic loss due to reduced crop yield and quality.

Control of plant virus diseases took a major step forward when it was shown that the tobacco mosaic virus ("TMV") coat protein ("CP") gene that was expressed in transgenic tobacco conferred resistance to TMV. The concept of pathogen-derived resistance ("PDR"), which states that pathogen genes that are expressed in transgenic plants will confer resistance to infection by the homologous or related pathogens, was introduced at about the same time. Since then, numerous reports have confirmed that PDR is a useful strategy for developing transgenic plants that are resistant to many different viruses. However, additional modes of protecting plants against virus disease are needed.

Recessive disease resistance genes are widely deployed in agriculture and are common in nature. However, not much is understood about the identity of naturally occurring recessive disease resistance genes in plants. Plant disease resistance conferred by recessive genetic factors has received limited attention relative to dominant R genes, despite their durability and prevalence in nature. Thus, there is a need to identify, isolate, and clone plant host genes whose gene product is essential for pathogenesis. This knowledge would be useful in that it would enable one to engineer disease resistance with the various gene silencing methods available in the art.

Potyviruses comprise approximately 30% of all known plant viruses and as a group are very destructive in agriculture. The family Potyviridae is characterized by a monopartite single-stranded positive sense RNA genome with a covalently-bound viral-encoded protein (VPg) attached at the 5′ terminus and a 3′ poly-A tract. The genome is approximately 10 kb in length and is translated as a polyprotein which is subsequently cleaved into smaller polypeptides by viral-encoded proteases. Based on similarities in genome structure, including conserved order and function among homologous replication proteins, potyviruses have been assigned to the proposed picorna-like superfamily of viruses, which includes many important human and animal pathogens, such as poliovirus and foot-and-mouth disease virus.

Potyvirus infection requires the interaction of host factors with viral proteins and RNA for replication and systemic spread. Although much is known regarding the functions of the individual potyvirus proteins and RNA structures in viral replication and movement, very little is understood about the identity and functions of host factors that are required for potyviral infection. Towards this end, the identification of naturally occurring host mutations that result in viral resistance and display monogenic recessive inheritance should define an important resource. The "negative model" of plant virus resistance predicts that a recessive resistance gene may represent a deleted or defective host protein that is essential for viral infection but is dispensable for the host. Recessive resistance is especially prevalent for potyviruses, comprising approximately 40% of all known resistance genes. Many of these genes, including the *Capsicum* resistance gene *pvr1*, have been used successfully for decades in crop breeding programs as effective and stable sources of resistance.

The potyviral NIa protein, also known as VPg-Pro, is comprised of an N-terminal VPg and C-terminal protease and participates in several replicative and proteolytic functions during potyvirus infection. The central region of VPg has been shown to be crucial in race-specific replication, cell-to-cell and long-distance movement functions in relation to recessive potyvirus resistance genes. The importance of NIa in potyvirus replication and movement has also prompted studies to identify host factors that interact with this protein using *in vitro* interaction assays. One study showed strong interaction in yeast two-hybrid assays between *Tobacco etch virus* (TEV) NIa and translation initiation factor eIF4E isolated from tomato and tobacco. Strong interactions have also been observed between *Arabidopsis thaliana* eIF4E or eIF(iso)4E and *Turnip mosaic virus* (TuMV) VPg-Pro both in yeast two-hybrid and ELISA-

based *in vitro* binding assays. Furthermore, the interaction of *Arabidopsis* eIF(iso)4E and TuMV VPg-Pro correlated with viral infectivity.

The present invention is directed to overcoming these deficiencies in the art.

The objection to the specification is respectfully traversed in view of the above amendment to the specification.

The objection to claim 53 is respectfully traversed in view of cancellation of this claim.

The rejection of claim 58 is under 35 U.S.C. § 101 for being directed to non-statutory subject matter is respectfully traversed in view of the above amendments.

The rejection of claim 53 under 35 U.S.C. § 112 (1st para.) for failure to satisfy the written description requirement is respectfully traversed in view of the cancellation of this claim.

The rejection of claims 50-58 under 35 U.S.C. § 112 (1st para.) for lack of enablement is respectfully traversed.

The United States Patent and Trademark office ("PTO") acknowledges that the present application is enabling for claims directed to a method of imparting virus resistance to plants expressing a heterologous eIF4E where the heterologous eIF4E comprises the amino acid sequence of SEQ ID NO: 2 which contains at least one substitution of T51A, P66T, V67E, K71R, L79R, G107P, or D109R. However, the PTO does not regard the present application as providing reasonable enablement for any heterologous eIF4E that is at least 85% similar to SEQ ID NO: 2 with at least one of the above substitutions. This rejection is overcome by the above amendments to claim 50 by which 95% similarity to the amino acid sequence of SEQ ID NO: 2 together with one of the above substitutions is required by the claims. As a result of these amendments, the claims now call for a much more circumscribed group of nucleic acid molecules where specific mutations are identified and discussed (see paragraphs [0101] and [0102]). As a result, the claimed invention is fully enabled by the present application.

Therefore the rejection of claims 50-58 for lack of enablement is improper and should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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